9; page 16, line 14 through page 18, line 3; page 30, line 22 through page 31, line 7; and page 38, lines 27-28. Support for new claim 30 may be found *inter alia* in the application as originally filed on page 8, line 25 through page 9, line 16; page 10, line 19 through page 11, line 18; and page 38, lines 27-28. Accordingly, applicants respectfully request that the amendment be entered.

Rejections under 35 U.S.C. §102(b)

On page 2 of the October 2, 2002 Office Action, the Examiner rejected claims 1 and 2 under 35 U.S.C. §102(b) as being anticipated by Cancroft et al. (Radiology 106: 441-444, 1973), as evidenced by Socolow et al. (Endocrinology 80: 337-344, 1967), Tazebay et al. (Nature Medicine 6: 871-878, 2000), Spitzweg et al. (Journal of Clinical Endocrinology 83: 1746-1751, 1998), and Eskandari et al. (Journal of Biological Chemistry 272: 27230-27238, 1997).

The Examiner stated that Cancroft et al. teach a method for differentiating benign and malignant masses in the breast tissue of a subject which comprises administering ^{99m}Tc-pertechnetate to the subject, and that ^{99m}Tc-pertechnetate is transported into the cell via mgNIS by a mechanism involving binding of the agent to the transporter. The Examiner stated that Eskandari et al. propose that the mechanism by which the thyroid gland sodium/iodide symporter (tgNIS) transports substrate, e.g., iodide, ^{99m}Tc-pertechnetate, and most other monovalent anions involves binding of the anion to the symporter, that the mechanism by which mgNIS transports anions such as ^{99m}Tc-pertechnetate is deemed the same as the mechanism by which tgNIS does so, absent a showing of any difference, and accordingly that the agent of the prior art is deemed the same as the agent of the instant claims, absent a showing of any difference. In an Office Action dated April 24, 2001, the Examiner had previously stated that Socolow et al. provide evidence that ^{99m}Tc-pertechnetate is selectively taken up by the thyroid gland by a mechanism that resembles

the mechanism by which radioiodide is taken up by the cells, that Tazebay et al. indicate that ^{99m}Tc-pertechnetate is selectively taken up by cells that express NIS, and that Spitzweg et al. provide evidence that the ability of thyroid tissue to selectively concentrate radioiodide (and ^{99m}Tc-pertechnetate) is dependent on the activity of NIS, which is commonly expressed in breast tissue also.

Applicants respectfully traverse this rejection and maintain that the claimed invention is patentable over the cited references. Cancroft et al. reported that ^{99m}Tc-pertechnetate images of the breast may be of value as a supplemental approach in the diagnosis of breast malignancy. In contrast, claim 1 as amended is directed to a method for detecting the presence or absence of breast cancer in a non-lactating subject, comprising determining whether or not mammary gland sodium/iodide symporter (mgNIS) is expressed in breast tissue of the subject, wherein expression of mgNIS in the breast tissue is detected using an antibody, or a fragment thereof, specific for mgNIS, and expression of mgNIS in the breast tissue is indicative of the presence of breast cancer in the subject, and no expression of mgNIS in the breast tissue is indicative of the absence of breast cancer in the subject. New claim 30 is directed to a method for detecting the presence or absence of breast cancer in a non-lactating subject, comprising determining whether or not mgNIS is expressed in breast tissue of the subject, wherein expression of mgNIS in the breast tissue is detected *in vitro* using at least one nucleic acid probe that specifically hybridizes to nucleic acid encoding mgNIS, and expression of mgNIS in the breast tissue is indicative of the presence of breast cancer in the subject, and no expression of mgNIS in the breast tissue is indicative of the absence of breast cancer in the subject. Applicants further note that Cancroft et al. do not even teach the existence of mgNIS, let alone the use of specific antibodies or nucleic acid probes for detecting the expression of mgNIS.

Applicants maintain that Cancroft et al. do not teach the claimed invention.

Accordingly, in view of the amendments and remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Objection to claims 4-6

On page 4 of the October 2, 2002 Office Action, the Examiner objected to claims 4-6 as being in improper because the claims depend from a canceled claim.

In response, applicants have canceled claims 4 and 5 and amended claim 6 to depend from claim 1. Accordingly, applicants respectfully request that the Examiner withdraw this objection.

Rejection under 35 U.S.C. §112, first paragraph

On page 4 of the October 2, 2002 Office Action, the Examiner rejected claims 7-9 and 29 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner stated that claims 7-9 and 29 are drawn to the method of claim 1 wherein the expression of mgNIS is detected using at least one nucleic acid probe. The Examiner alleged that the teachings of the specification cannot be extrapolated to the enablement of the claimed invention because a nucleic acid probe is not expected to bind to mgNIS, and the method has not been exemplified.

In response, applicants have deleted claim 7, added new claim 30, and amended claims 8-9 and 29 to depend from claim 30. Applicants note that claim 30 recites that the nucleic acid probe "specifically hybridizes to nucleic acid encoding mgNIS..." and does not require that the nucleic acid probe bind to mgNIS itself.

Applicants further note that the Examiner has in Office Actions issued on April 24, 2001 and December 13, 2001, rejected previous claim 7 under 35 U.S.C. §112, second paragraph, allegedly because the use of the term "hybridizes" renders the claim indefinite, and that the Examiner had at the same time suggested alternative claim language for applicants' consideration.

Applicants thank the Examiner for his previous suggestions. However, at the same time, applicants note that:

> The examiner's focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. 112, second paragraph is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. MPEP §2173.02.

Applicants also note that:

> Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and
>
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.
>
> MPEP §2173.02.

Applicants maintain that one of ordinary skill in the art would ascertain the stringency conditions required for the nucleic acid probe of claim 30 to specifically hybridize to nucleic acid encoding mgNIS. Applicants further maintain that the skilled artisan would readily understand that new claim 30 specifies that the expression of mgNIS in breast tissue is detected using at least one nucleic acid probe that specifically hybridizes to nucleic acid

encoding mgNIS, and that the "metes and bounds" of the invention are clear from the language of claim 30 as well as from the language of dependent claims 8, 9, and 29.

Accordingly, in view of the amendments and remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Supplemental Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the references which are listed on the attached form PTO/SB/08A-B (substitute for form 1449/PTO) (**Exhibit A**) and attached hereto as **Exhibits 1-3**. The attached references were cited in a Supplementary Partial European Search Report dated September 5, 2001 in connection with related European Patent Application No. 97903839.5. A copy of the Search Report is attached hereto as **Exhibit 4**.

Applicants are submitting the subject Supplemental Information Disclosure Statement pursuant to 37 C.F.R. §1.97(c)(2) before the mailing of any of a Final Office Action under 37 C.F.R. §1.113, a Notice of Allowance under 37 C.F.R. §1.311, or an action that otherwise closes prosecution in the application. A check for $180.00 is enclosed to cover the fee for submitting an Information Disclosure Statement pursuant to 37 C.F.R. §1.97(c)(2).

Conclusion

In light of the claim amendments and the above remarks, applicants respectfully request withdrawal of all objections and rejections and passage of currently pending claims 1, 2, 6, 8, 9, 29, and 30 to allowance. If there are any minor matters that would prevent allowance of the claims, applicants request that the Examiner contact the undersigned attorney.

It is believed that no fee, other than the enclosed $180.00 fee for submitting an Information Disclosure Statement, is required to maintain the pendency of the subject

application. However, if there are any unanticipated fees required to maintain the pendency of this application, the PTO is authorized to withdraw those fees from Deposit Account 01-1785. Overcharges may also be credited to Deposit Account 01-1785.

Respectfully submitted,

AMSTER, ROTHSTEIN & EBENSTEIN
Attorneys for Applicants
90 Park Avenue
New York, New York 10016
(212) 697-5995

Dated: New York, New York
December 20, 2002

By: _____
Craig J. Arnold
Registration No. 34,287
Alan D. Miller
Registration No. 42,889

Marked-Up Pending Claims as Amended in Reply to October 2, 2002 Office Action
U.S. Patent Application No. 09/519,959
Additions are underlined and deletions are bracketed.

--1. (Four times amended) A method for detecting the presence or absence of breast cancer in a non-lactating subject, comprising determining whether or not mammary gland sodium/iodide symporter (mgNIS) is expressed in breast tissue of the subject [using an agent that binds to mgNIS], wherein

[binding of the agent in the breast tissue is indicative of] expression of mgNIS in the breast tissue <u>is detected using an antibody, or a fragment thereof, specific for mgNIS,</u> and

expression of mgNIS in the breast tissue is indicative of the presence of breast cancer in the subject, and no expression of mgNIS in the breast tissue is indicative of the absence of breast cancer in the subject.--

2. The method of Claim 1, wherein the expression of mgNIS is detected *in vitro* or *in vivo*.

--6. (Amended) The method of Claim [5] <u>1</u>, wherein the antibody is labeled with a detectable marker.--

--8. (Twice Amended) The method of claim [7] <u>30</u>, wherein the nucleic acid probe is DNA.--

--9. (Amended) The method of Claim [7] <u>30</u>, wherein the nucleic acid probe is labeled with a detectable marker.--

--29. (Amended) The method of claim [7] <u>30</u>, wherein the nucleic acid probe is RNA.--

--30. (New) A method for detecting the presence or absence of breast cancer in a non-lactating subject, comprising determining whether or not mammary gland sodium/iodide symporter (mgNIS) is expressed in breast tissue of the subject, wherein

expression of mgNIS in the breast tissue is detected *in vitro* using at least one nucleic acid probe that specifically hybridizes to nucleic acid encoding mgNIS, and

expression of mgNIS in the breast tissue is indicative of the presence of breast cancer in the subject, and no expression of mgNIS in the breast tissue is indicative of the absence of breast cancer in the subject.--